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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: EMBIL et al.	Confirmation No: 2411
Appl. No.	: 10/761,390	
Filed	: January 22, 2004	
Title	: TOPICAL PHARMACEUTICAL AND/OR COSMETIC DISPENSE SYSTEMS	
TC/A.U.	: 1614	
Examiner	: Not Assigned Yet	
Docket No.:	: EMBI3001/REF	
Customer No:	: 23364	

COMPLETION OF CLAIM FOR PRIORITY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants hereby submit the official certified copy of priority document number GB 0301577.3 in connection with the above identified application, benefit of which is claimed in the Declaration and the Application Data Sheet of this application. The Examiner is most respectfully requested to acknowledge receipt of this certified copy in the next Official Action.

Respectfully submitted,

BACON & THOMAS, PLLC

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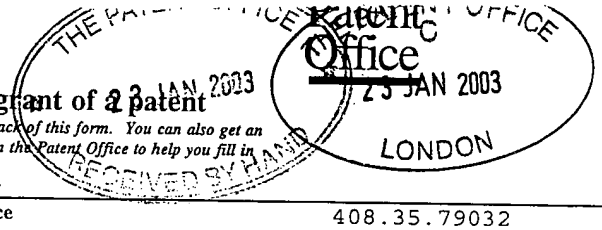
REF:kdd
Completion of Claim for Priority.wpd

April 27, 2004

(Rule 10)



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1. Your reference — 408.35.79032

2. Patent application number *(The Patent Office will fill in this part)* — 0301577.3 — 23 JAN 2003

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

EDKO PAZARLAMA TANITIM LTD. STI.
(EDKO TRADING AND REPRESENTATION CO. LTD.)
Birahane Sokak No. 40
80223 Istanbul
Turkey

Patents ADP number *(if you know it)* — 8551095001

24JAN03 E779479-1 000027
P01/7700 0.00-0301577.3

If the applicant is a corporate body, give country/state of incorporation — Turkey

4. Title of the invention — Topical Pharmaceutical and/or Cosmetic Dispense Systems

5. Name of your agent *(if you have one)* — Frank B. Dehn & Co.

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

179 Queen Victoria Street
London
EC4V 4EL

Patents ADP number *(if you know it)* — 166001 ✓

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

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11. I/We request the grant of a patent on the basis of this application.

Frank B. Dehn & Co. - Agents for the Applicant — Signature — Date 23 January 2003

12. Name and daytime telephone number of person to contact in the United Kingdom

J.C. Marsden
020 7206 0600

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Signed Andrew Gerry

Dated 24 February 2004

79032.620

Topical Pharmaceutical and/or Cosmetic Dispense Systems

This invention relates to systems for dispensing topical pharmaceutical and/or cosmetic formulations, e.g. pharmaceutical formulations for the treatment of dermatological conditions such as acne and rosacea.

It has long been the case that pharmaceutical formulations, typically in the form of creams or gels suitable for topical administration, have been used to combat skin disorders which are caused by the inflammation of sebaceous glands and/or skin follicles and which may result in conditions such as acne and rosacea.

Many previous treatments for these disorders can be found in the literature and often comprise topically administrable organic peroxides and/or antibiotics. Thus, for example, formulations for the treatment of skin disorders comprising benzoyl peroxide are described in US-A-3535422, US-A-4056611, US-A-4318907, US-A-4923900, US-A-4387107 and US-A-4228163.

Other patents have disclosed formulations comprising an antibiotic for the treatment of skin disorders such as acne and rosacea. US-A-3969516, for example, describes the use of the topical antibiotic clindamycin for the treatment of acne. Other antibiotics which have been used in the treatment of skin disorders include erythromycin and tetracyclines.

Still further patents disclose formulations comprising a combination of an organic peroxide and an antibiotic for the treatment of skin disorders. GB-A-2088717, US-A-4411893, US-A-4692329 and GB-A-1594314, for example, describe combinations of the antibiotic erythromycin with various organic peroxides as formulations for the treatment of acne or other skin disorders. US-A-4607101 discloses a formulation for the treatment of acne vulgaris comprising a carbamide

peroxide in combination with a topical antibiotic.

It has been found that combinations of an antibiotic with an organic peroxide may be more effective in the treatment of skin disorders than either the antibiotic or the peroxide alone - see, for example, US-A-4497794.

Benzoyl peroxide, like other organic peroxides, exerts an antibacterial effect via its strong oxidising properties. This chemical property of peroxides, however, can reduce the stability of such peroxide-containing two component formulations, since oxidative interaction with the second (e.g. antibiotic) component may lead to loss of potency of both active ingredients.

Benzamycin® is a topical gel for the treatment of acne comprising a combination of 3% erythromycin, as a topical antibiotic, and 5% benzoyl peroxide, as an antibacterial, keratolytic and desquamating agent. This combination, however, is unstable at room temperature for the above reason, so that Benzamycin® rapidly loses its pharmaceutical effectiveness if stored at ambient temperature.

In order to prolong the pharmaceutical effectiveness of Benzamycin® it may be formulated by a pharmacist as and when required, thereafter being stored under refrigeration. However, this limits the product to being sold in a pharmacy and may also lead to variation in the final composition. Thus the pharmacist is required firstly to dissolve the erythromycin in an alcohol and then to add the resulting solution to a gel containing the benzoyl peroxide, thereafter stirring the mixture until it is homogeneous in appearance. Accordingly, variations in the alcohol used for this purpose may lead to variability in the product; if the mixing is not complete, partially dissolved or undissolved drug aggregates may remain, which may lead the product to feel gritty on application. Moreover, it may be impractical for a patient to store Benzamycin® in

a refrigerator (for example, when the patient is travelling or does not have access to a refrigerator); the need for refrigeration may also reduce patient compliance, since the application of a cold topical formulation may well be unpleasant.

Various attempts have been made to overcome the instability of formulations such as Benzamycin®. US-A-5446028, US-A-5767098 and US-A-6013637, for instance, disclose formulations further comprising a stabilising agent such as dioctyl sodium sulfosuccinate. US-A-5466446 discloses a method for preparing a reportedly stable formulation comprising clindamycin and benzoyl peroxide by controlling the ratio of each active ingredient. The proprietor of this patent markets a product under the name Clindoxyl® Gel which contains benzoyl peroxide and clindamycin in the ratio of 5:1 and which has a shelf-life of 60 days at room temperature. The product is, however, required to be kept refrigerated prior to being dispensed, which is inconvenient.

US-A-6117843 discloses compositions wherein the ratio of organic peroxide to antibiotic is a factor in achieving stability in the final composition. According to this patent a composition comprising benzoyl peroxide and clindamycin is prepared by a pharmacist by mixing an aqueous solution of clindamycin, typically having a pH of 5 to 6.5, with an aqueous suspension of benzoyl peroxide, typically having a pH of about 4 to 5. The benzoyl peroxide suspension preferably also contains a gelling agent with a pH-dependent viscosity, so that the viscosity of the product is increased when the two components are mixed. A gel composition is therefore obtained which is reported to be stable for around three months at room temperature.

US-A-6462025 discloses that separate antibiotic and benzoyl peroxide compositions may be packaged within and dispensed from a common dispenser such as a dual chamber

storage device. In this way the active ingredients are kept apart during storage, being dispensed and mixed as required immediately prior to application to the skin; long shelf life may thereby be achievable.

This patent requires at least the antibiotic to be formulated in a substantially anhydrous composition comprising a polar solvent such as a polyol and a thickening agent which is a (meth)acrylic acid polymer or a poly(meth)acrylamide. It is suggested that the benzoyl peroxide may also be presented in a substantially anhydrous polar solvent- and thickening agent-containing composition; for reasons of "cosmetic elegance" this should preferably have a viscosity differing by no more than 25% from that of the antibiotic composition.

Such thickened substantially anhydrous gels and like compositions are not, however, ideal medicaments for the treatment of skin disorders, since their use may lead to blockage of pores and/or the bases of hair follicles in a patient's skin, thereby potentially exacerbating conditions such as acne.

The present invention is based on the finding that dual (or multi) formulation topical pharmaceutical products having significantly improved effects in the treatment of dermatological conditions such as acne may be obtained by using separate water-based formulations for each active ingredient. The improvement is achieved by incorporating at least one of the active ingredients into a microsponge delivery system and by using aqueous carrier bases with substantially the same lipophilicity in each of the formulations.

Thus it has been found that the use of aqueous carriers optimises performance of microsponge delivery systems, both by ensuring slow continuous release of active ingredient from within the lipophilic environment of the microsponges and by enhancing the ability of the microsponges to absorb excess oil and sebum from the

skin. This latter property is highly beneficial given that excess sebum content of the skin leads to blockage of pores and hair follicle bases, which in turn may lead to inflammation of the skin and development of acne.

The requirement for the formulations to comprise carrier bases with substantially the same lipophilicity is also an important feature of the invention which may facilitate particularly ready, uniform and thermodynamically favourable mixing of the formulations. More importantly, it ensures consistent release of active ingredient from the microsponge delivery system or systems. Thus the release properties of such systems are dependent on the physical properties of the carrier in which they are dispersed, including pH and viscosity; the degree of lipophilicity is particularly important since it affects the partition coefficient of active ingredient between the microsponges and the carrier and thus controls the rate of release of active ingredient from the microsponges into the carrier and thus to the skin. By using carriers with substantially identical lipophilicity the products may be designed to ensure that a desired rate of release from the microsponge delivery system is consistently achieved after the formulations have been mixed and applied to the skin.

Excellent storage stability (e.g. six months or more, preferably in excess of 12, 18 or even 24 months) may be achieved by presenting the active ingredients in separate formulations which may be mixed immediately prior to, during or following application to the skin of a patient. In the case of systems involving oxidising antibacterials such as benzoyl peroxide and antibiotics such as clindamycin, highly efficacious formulations with a storage life in excess of two years at ambient temperature may be prepared in this way. The principle may also be applied to any other topical pharmaceutical and/or cosmetic formulations involving components which may potentially be mutually incompatible, e.g. as a

result of chemical interaction. It is also generally applicable to dual and multi formulation topical pharmaceuticals and cosmetics in which at least one of the formulations involves a microsponge delivery system.

Thus according to one aspect of the present invention there is provided a pharmaceutical and/or cosmetic product comprising first and second active ingredient-containing formulations for topical administration to a patient, wherein said product includes storage means whereby said formulations are maintained separately prior to dispense, together with dispense means which permit said formulations to be dispensed from said storage means, characterised in that (i) an active ingredient in at least one of said formulations is contained within a microsponge delivery system and (ii) both of said formulations comprise aqueous carrier bases having substantially the same lipophilicity.

It will be appreciated that the invention embraces products comprising more than two formulations as defined above provided that these are each separately maintained in appropriate storage means prior to dispense, that all comprise aqueous carrier bases having substantially the same lipophilicity, and that at least one active ingredient is contained within a microsponge delivery system.

The storage means within products of the invention may, for example, comprise separate chambers or compartments of a dual- or multi- chamber or compartment dispense device, for example side-by-side collapsible tubes, syringe barrels or other forms of container with appropriate dispense valves, pistons, plungers or the like. Alternatively the storage means may take the form of a pouch containing a single unit dose of each formulation; such unit dose pouches may, for example, be made of composite materials such as a metal (e.g. aluminium) foil having a plastics material (e.g.

polyethylene or polyvinyl chloride) inner lining, with the pouch having separate parts for each formulation.

The dispense means are preferably such that the formulations are dispensable in a controllable (e.g. predetermined) ratio, for example in equal amounts or in other relative amounts as determined to optimise the efficacy of the combined formulation after mixing. In this way variations in the composition of the mixed product may be substantially reduced or eliminated. Thus, for example, side-by-side tube containers may be progressively emptied by turning a common winding key adapted to engage and roll up their distal ends, or the plungers of side-by-side syringes may be mutually linked together. It will be appreciated that the respective cross-sectional areas of such containers may be selected to ensure that the formulations are dispensed in the desired ratio for a given movement of a linked dispensing actuator.

In the case of unit dose pouches, the ratio of the formulations is predetermined at the filling stage, so that the dispense means need comprise no more than corners or edges which may be cut off or torn off to permit the formulations to be squeezed out.

In general it is convenient to dispense the formulations of a product of the invention in equal amounts, for example each in volumes in the range 2-5 ml, advantageously 2.5-4.5 ml, preferably 3-4 ml.

In a preferred product according to the invention, first and second formulations are respectively presented in the chambers of a dual chamber dispense system of the type described in EP-A-0644219, the contents of which are incorporated herein by reference. Such a system has two side-by-side chambers, each equipped with a dispense valve; these are operated by adjacent actuators so as to dispense the formulations either simultaneously or separately as desired. Suitable dispense systems, e.g. having chambers which are each capable of holding about

15 ml of formulation, are available from Maplast S.r.l., Via Pasublo 3, Tradate 21049 VA, Italy. The respective dimensions of the dispense means may be chosen to provide dispense of the respective formulations in a predetermined ratio.

The product may include mixing means such that the formulations are admixed during dispense. Thus, for example, the points of dispense for each of the storage means may be connected to a single duct and/or nozzle outlet; this may, for example, be spirally grooved on its inner surface in order to enhance the efficiency of mixing.

Alternatively the formulations may be dispensed separately and mixed by the patient. Thus, for example, a dispense system of the type described in the above-mentioned EP-A-0644219 may be fitted with separate duct/nozzle outlets for dispense of each formulation. Separate operation of each actuator will deliver appropriate relative amounts of the formulations, e.g. onto the hand or directly onto an affected area of skin; the formulations may then be mixed by the patient, e.g. by rubbing. It will be appreciated that such embodiments may be preferred to products which include mixing means in cases where the active ingredients are mutually reactive to the extent that they may generate toxic or otherwise undesirable byproducts while residual mixed formulations stand in a common duct and/or nozzle between successive dispense operations.

In one class of preferred products according to the invention, the first formulation is an aqueous topical cream or gel carrier base containing an antibacterial and/or keratolytic agent incorporated into a microsponge delivery system, and the second is an aqueous carrier base having substantially the same lipophilicity and containing a topical antibiotic; if desired, the antibiotic may also be contained within a microsponge delivery system.

Preferred antibacterial agents include salicylic acid and organic peroxides, especially benzoyl peroxide. Salicylic acid may, for example, be present in such a first formulation in an amount of 0.2-40% w/w, advantageously 1-30% w/w, preferably 2-20% w/w. Organic peroxides may, for example, be present in amounts of 0.2-40% w/w, advantageously 2-30% w/w, preferably 4-20% w/w. Keratolytic agents which may be used include retinoids such as retinoic acid and salts and esters thereof, for example in amounts of 0.01-1% w/w, advantageously 0.025-0.75% w/w, preferably 0.05-0.5% w/w.

It will be appreciated that the amount of antibacterial and/or keratolytic agent (and of all other active ingredients) should be selected to give a desired end product concentration following the overall dilution of each ingredient which will occur when the formulations are mixed.

Microsponge delivery systems useful in products of the invention may, for example, be as described in WO-A-8810132, US-A-4873091, US-A-4690825 and EP-A-0306236. Thus, for example, antibacterial agents such as benzoyl peroxide may be formulated in similar manner to the product marketed in the USA under the tradename Exact® and by the present applicant in Turkey under the name Aksil®; benzoyl peroxide-containing microsponges are described in, for example, US-A-5879716. Similar microsponges containing retinoic acid are described in US-A-5955109. Loading of the active ingredient may take place via either a one-step or two-step process, e.g. as described in US-A-4690825 and US-A-5145675 respectively, whereafter the resulting microsponges may be suspended in the desired aqueous carrier base.

An advantage of such systems is that release of the antibacterial and/or keratolytic agent from the microsponges can be made to occur quite slowly, conveniently with onset being triggered by dispense

and/or application with rubbing of the formulations onto the skin. The concentration of the agent in the carrier base at any time may consequently be low, minimising possible irritant side-effects whilst maintaining a therapeutically effective concentration. Similar advantages may accrue if the topical antibiotic is also contained within its own microsponge delivery system.

The microsponges of the microsponge delivery system may be composed of a wide range of materials, including both synthetic polymers and natural substances such as cellulose or gelatin. The choice of material forming the microsponge delivery system may depend upon the intended methods by which the entrapped antibacterial or other agent is to be released. Such methods are described in J. Microencapsulation (1996), 13(5), 575-588 and include but are not limited to diffusion, compression, dissolution or melting.

Preferably, entrapped antibacterial and/or keratolytic agent is released from the microsponge delivery system by diffusion from the pores of the microsponges into the carrier. The rate of diffusion will depend on the partition coefficient of the antibacterial and/or keratolytic agent (and any other entrapped active ingredients) between the polymer forming the microsponge delivery system and the carrier.

Microsponges containing agents such as benzoyl peroxide or retinoic acid will typically release sufficient of the agent into the carrier base during storage, dispense and/or application to provide a therapeutically effective initial concentration of agent in the formulation as applied to the skin. Agents such as salicylic acid, however, may not undergo such ready initial release from a microsponge delivery system because of their different lipophilicity; it may therefore be advantageous to include a proportion of "free" agent in the carrier base (e.g. up to 25% w/w of the total content of the agent) to provide the required

initial therapeutically effective concentration and to induce release of agent from the microsponges.

The diameter of the porous particles which comprise the microsponge delivery system may, for example, be in the range 1 to 1000 microns, e.g. 4 to 300 microns, such as 5 to 100 microns. It is preferred, however, that the particle size is less than 30 microns, e.g. 10 to 25 microns, since particles larger than 30 microns can impart a 'gritty' feel to the formulation, which may decrease patient compliance.

The surface area of the porous particles which comprise the microsponge delivery system may, for example, range from 1 to 500 m^2/g, e.g. 20 to 200 m^2/g; the total pore volume may, for example, be in the range 0.3 to 4.0 cm^3/g, e.g. 0.6 to 2.0 cm^3/g. Pore volume may have a significant effect on the rate of release of the entrapped antibacterial and/or keratolytic agent, and may affect the migration of the agent from the microsponge delivery system into the carrier in which the microsponge delivery system is dispersed. Thus the diameter (and hence volume) of the pores has a direct impact on the release of the agent, as well as on the amount of agent that can be entrapped within the microsponge delivery system.

The microsponge delivery system may be made by suspension polymerisation, preferably crosslinking polymers such as polyolefins, for example polyethylene, polystyrene and polydicyclopentadiene; polyacrylate esters, for example optionally alkoxylated C_{1-10} alkyl, cycloalkyl, aryl or aralkyl esters of polyacrylic or polymethacrylic acids; polyvinyl esters, for example polyvinyl acetate or polyvinyl laurate; polyvinyl ketones, for example polyvinylmethyl ketone; and polyvinyl ethers, for example polyvinyl propyl ether. The most commonly used crosslinking agents are divinylbenzene for polystyrene polymers and ethylene glycol dimethacrylate for polymethacrylates.

It will be appreciated that the level of hardness of the particles of the microsponge delivery system may be varied widely by appropriate selection of the polymer composition, degree of crosslinking etc. It is preferred that the particles are elastically compressible so that after application of the formulation to an infected area, the application of gentle pressure, for example by rubbing, may induce release of the entrapped antibacterial and/or keratolytic agent into the carrier and thus to the skin.

In addition to the antibacterial and/or keratolytic agent, the porous microspheres of the microsponge delivery system may entrap a wide range of other ingredients such as emollients, fragrances, antioxidants, essential oils, sun screens, anti-infective, antifungal and anti-inflammatory agents, more particularly fragrances and antioxidants such as butylated hydroxyl anisole, butylated hydroxyl toluene, alkyl gallates (e.g. propyl gallate), or tocopherols.

Preferred topical antibiotics useful in the second formulation of the aforementioned class of preferred products include tetracyclines (e.g. formulated at concentrations of 0.2-20% w/w, advantageously 1-12% w/w, preferably 2-4% w/w), erythromycin (e.g. formulated at concentrations of 2-30% w/w, advantageously 6-20% w/w, preferably 8-12% w/w), and clindamycin (e.g. formulated at concentrations of 0.02-20% w/w, advantageously 0.2-10% w/w, preferably 1.6-5.2% w/w). Again allowance should be made for the overall dilution of individual active ingredients which will occur when the formulations are mixed. Where appropriate, e.g. for solubility or distribution considerations, corresponding salts or esters, e.g. mineral acid addition salts such as clindamycin hydrochloride or phosphate, or carboxylic acid esters such as erythromycin propionate, stearate or ethylsuccinate may also be used.

The term "aqueous carrier base" as used herein

denotes a topical carrier base in which water is the major component, e.g. being present in amounts in excess of 50, 55, 60, 65 or 70% w/w; such carriers may typically comprise aqueous creams, gels, lotions or ointments.

The carriers may, for example, include conventional formulating ingredients selected from lipophilic base materials (for example fatty (e.g. C_{10-30}) alcohol esters of saturated or unsaturated fatty (e.g. C_{10-30}) acids, such as cetyl ricinoleate; fatty acid esters of sterols such as cholesterol or lanosterol; emollient silicon oils, e.g. polysiloxanes such as dimethicone or cyclomethicone; or terpenes such as α-bisabolol), hydrophilic base materials (for example polyethylene glycols, hereinafter referred to as PEGs), stabilisers and/or surfactants (for example fatty acids such as palmitic or stearic acid; fatty alcohols such as cetyl or stearyl alcohol; amphiphilic fatty esters, e.g. fatty alcohol esters of mineral acids such as sodium lauryl sulphate, fatty acid esters of polyols such as glyceryl dilaurate or caprylic/capric triglyceride; PEGylated fatty alcohols, e.g. PEG lauryl ethers such as laureth-4; PEGylated sorbitan esters with fatty acids such as oleic, lauric, palmitic or stearic acid, e.g. as in Tween® surfactants; PEGylated sterols such as PEG-10 soya sterol; polysaccharides such as xanthan gum; proprietary products such as emulsifying wax; or thickening polymeric stabilisers, e.g. polyacrylamide-based products such as Sepigels®), humectants (for example diols or polyols such as propylene glycol or glycerol), viscosity modifiers (for example saccharides such as sorbitol), thickeners (for example colloidal or fumed silica or silicates such as magnesium aluminium silicate), preservatives (for example antimicrobials or antifungals such as methyl paraben, propyl paraben, benzyl alcohol, phenoxyethanol or germaben II; or antioxidants such as vitamin E, ascorbyl palmitate or

butylated hydroxytoluene), pH regulators (for example buffers, e.g. acid/salt combinations such as citric acid/sodium citrate; or bases such as triethanolamine), or anticoagulants (for example disodium edetate).

As noted above, the lipophilicity of a formulation affects the partition coefficient of active ingredient contained within a microsponge delivery system between the microsponges and the carrier. The requirement for the carriers within a particular product according to the invention to have substantially the same lipophilicity may therefore be tested and quantified by determining the partition coefficient in respect of each carrier base; the requirement is met if the partition coefficients vary by no more than 10%, advantageously by no more than 5%, preferably by no more than 2.5%. It is also preferred that the individual water contents and viscosities of the formulations within a particular product vary by no more than these limits, since this may enhance ease and uniformity of mixing of the formulations during or after dispense. In general the viscosities of the formulations may advantageously be in the range 100,000-200,000 cps, e.g. 125,000-175,000 cps.

The carriers within a particular product may advantageously contain essentially the same ingredients or close analogues, homologues or equivalents thereof, in amounts appropriate to ensure the desired levels of lipophilicity etc. Where it is desired substantially to match the viscosities of the formulations within a product, it will be appreciated that the presence of microsponges in a formulation may have a significant viscosity increasing effect, particularly if the microsponge content is relatively high (for example as may be required if the level of entrapment of active ingredient in the microsponges is relatively low). It may therefore be desirable to increase the relative amounts of viscosity enhancing agents (e.g. polysaccharides such as xanthan gum or thickening agents

such as silica or silicates) and/or to reduce the amount of relatively low viscosity components such as glycerol or sorbitol in a corresponding non-microsponge formulation in order to compensate for this.

The pharmaceutical formulations in products of the present invention may be manufactured by methods conventionally known for the manufacture of pharmaceutical creams or gels. One suitable method of manufacture includes the steps of preparing an aqueous solution of the water-soluble ingredients, mixing this solution together with the hydrophobic ingredients, homogenising the resulting mixture and thereafter adding the active ingredient (e.g. antibacterial agent or antibiotic). The resulting cream or gel may then be filled into the appropriate storage means of the product.

To use a product of the present invention, a patient may simply activate the dispense means (e.g. by depressing a pump or plunger) and collect the formulation(s) dispensed, e.g. in his hand. If necessary, the patient may then mix the formulations to obtain a combination product which is applied to the area(s) of skin to be treated. Formulations dispensed from the products of the invention are preferably applied on a regular basis, for example once or twice daily.

The contents of all publications, patents or otherwise, mentioned hereinbefore are herein incorporated by reference.

Claims

1. A pharmaceutical and/or cosmetic product comprising first and second active ingredient-containing formulations for topical administration to a patient, wherein said product includes storage means whereby said formulations are maintained separately prior to dispense, together with dispense means which permit said formulations to be dispensed from said storage means, characterised in that (i) an active ingredient in at least one of said formulations is contained within a microsponge delivery system and (ii) both of said formulations comprise aqueous carrier bases having substantially the same lipophilicity.

2. A product as claimed in claim 1 wherein the dispense means are such as to permit dispense of said formulations in controllable relative amounts.

3. A product as claimed in claim 1 or claim 2 wherein the storage means comprise side-by-side chambers each equipped with a dispense valve, said valves being operable by adjacently disposed actuators.

4. A product as claimed in claim 1 or claim 2 wherein the storage means comprise a unit dose pouch having separate parts for each formulation.

5. A product as claimed in any of the preceding claims wherein the dispense means are adapted to dispense said formulations separately.

6. A product as claimed in any of the preceding claims wherein the first formulation is an aqueous topical cream or gel carrier base containing an antibacterial and/or keratolytic agent incorporated into a microsponge delivery system and the second formulation is an aqueous

carrier base having substantially the same lipophilicity and containing a topical antibiotic.

7. A product as claimed in claim 6 wherein said keratolytic agent is a retinoid.

8. A product as claimed in claim 7 wherein said retinoid is retinoic acid.

9. A product as claimed in claim 6 wherein said antibacterial agent is salicylic acid or an organic peroxide.

10. A product as claimed in claim 9 wherein said organic peroxide is benzoyl peroxide,

11. A product as claimed in any of claims 6 to 10 wherein said antibiotic is erythromycin, clindamycin or a tetracycline.

12. A product as claimed in claim 11 wherein said antibacterial agent is benzoyl peroxide and said antibiotic is clindamycin.

13. A product as claimed in any of claims 6 to 12 wherein said topical antibiotic is contained within a microsponge delivery system.

14. A product as claimed in any of the preceding claims wherein said first and second formulations have substantially the same water content.

15. A product as claimed in any of the preceding claims wherein said first and second formulations have substantially the same viscosity.